Remarks

Claims 1-15, 17, and 19-28 were pending in this application, with claims 4-10 and 19-28 being withdrawn as being directed to non-elected invention(s). Claim 1 is amended herein. Claims 4-10 and 19-28 are hereby canceled without prejudice, as being drawn to non-elected inventions. New claims 29-32 are added herein. No new matter is introduced by these amendments. After entry of this Amendment, **claims 1-3, 11-15, 17, and 29-32** are pending in this application. Consideration and allowance of the pending claims is requested.

Claim Amendments/New Claims

Claim 1 is amended herein to recite "digitizing the fluorescence intensity; and quantifying the fluorescence intensity." Support for this amendment may be found in the specification, for example at paragraphs [0115]-[0116], [0126], and [0134]-[0135] (paragraph numbering as in U.S. Pat. Publication No. 2007/0202535-A1).

New claims 29-32 are also added herein. New claim 29 depends from claim 11 and recites "wherein the protein that interacts with a sugar chain is a lectin." Support for this claim may be found in original claim 11 and in the specification, for example at paragraphs [0054]-[0056]. New claim 30 depends from claim 12 and recites "wherein the evanescent wave is generated by total internal reflection of the excitation light." Support for claim 30 may be found in the specification, for example at paragraph [0073].

New claim 31 depends from claim 1 and recites "comparing the fluorescence intensity with a database of fluorescence intensities of known sugar chains; and determining the identity of the labeled sugar chain by selecting a sugar chain of known structure having a matching pattern of fluorescence intensity." Support for this claim may be found in the specification, for example at paragraphs [0075], [0078], and [0084]. Finally, new claim 32 is also added herein, which recites "a method for analyzing an interaction between a sugar chain and a protein that interacts with a sugar chain, comprising: contacting a sample comprising at least one fluorescently labeled glycoprotein with a glass slide comprising one or more lectin conjugated to the glass slide through an epoxy group of 3-glycidoxypropyl trimethoxysilane; applying an

excitation light to the substrate without washing the substrate; generating an evanescent wave by total internal reflection of the excitation light; and measuring intensity of emitted fluorescent light generated by the evanescent wave, wherein an increase in the emitted fluorescent light indicates the interaction between the fluorescently labeled glycoprotein and the lectin." Support for this claim may be found throughout the specification, for example, paragraphs [0021]-[0023] and Example 1 (paragraphs [0103]-[0124]).

Claim Rejections – 35 U.S.C. § 102

Claims 1-3, 11, 13, and 17 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Chan *et al.* (U.S. 2002/0192680). Applicants traverse to the extent the rejection is maintained in view of the amendments herein.

Chan *et al.* do not disclose all the limitations of claim 1, and therefore this reference cannot anticipate claims 1-3, 11, and 13. Claim 1 recites "contacting a *fluorescently labeled subject sugar chain or subject glycoconjugate* with a substrate onto which a protein that interacts with a sugar chain has been immobilized…" (emphasis added). Chan *et al.* do not disclose contacting a fluorescently labeled sugar chain or glycoconjugate with a substrate onto which a protein that interacts with a sugar chain is immobilized. The method of Chan *et al.* utilizes a change in the refractive index (red shift) of a semiconductor structure upon binding of a target molecule to a probe coupled to the semiconductor structure to detect a target-probe interaction (see, *e.g.,* Chan *et al.* at [0066]). Thus, the excitation light actually activates the substrate itself, rather than the analyte molecules, which are not labeled (see, *e.g.,* paragraph [0019] and Figure 6). Chan's method does not utilize a labeled probe or target molecule; the detectable signal is an intrinsic property of the semiconductor structure. Similarly, Example 6 of Chan *et al.*, describes detection of an interaction between an unlabeled lipopolysaccharide and an organic probe molecule (TWTCP; paragraph [0103]). Neither of these are fluorescently labeled, and the molecule immobilized on the substrate is *not* "a protein that interacts with a sugar chain…" as recited in pending claim 1. The only discussion of a fluorescently labeled molecule by Chan *et al.* is a fluorescently labeled *DNA* probe, which was utilized to confirm immobilization of DNA in the semiconductor structure (Chan *et al.* [0090]).

Interaction between fluorescent-labeled glycoconjugates and glycan-binding proteins immobilized on a substrate can be confirmed by addition of non-labeled inhibitory saccharides in a competitive assay. One way in which the differences between Chan *et al.* and the present claims can be illustrated is that such competitive assays can be carried out as described in the present application (*e.g.*, Figure 8). In contrast, competitive assays cannot be carried out using the method described by Chan *et al.* because the red shift occurs independently of whether analytes are labeled or unlabeled.

In addition, Applicants reassert the previously presented argument that Chan *et al.* do not disclose "measuring the intensity of an excited fluorescence after applying an excitation light *without washing the substrate*" (emphasis added). The Office asserts that Chan *et al.* do not specifically teach a washing step and that the description of a washing step at paragraph [0099] is merely exemplary. However, it is routine in the art of hybridization (*e.g.* nucleic acid-nucleic acid interaction) and protein-protein or protein-sugar interaction to include a washing step to decrease non-specific binding. Therefore, in the absence of specific teaching that a washing step is *not* required, one of skill in the art would understand that a washing step is included in such assays, even if it is not specifically recited.

Finally, Chan *et al.* do not disclose "digitizing the fluorescence intensity and quantifying the fluorescence intensity." Chan *et al.* merely describe detecting an increase in fluorescence when fluorescently labeled DNA is added to their array and that the fluorescence increases in the presence of increasing amounts of probe DNA (paragraph [0090]). Chan *et al.* acknowledge that their method utilizing fluorescent tagging provides *qualitative* results (paragraph [0090]), rather than quantitative results, as are achieved with the claimed methods.

Since Chan *et al.* do not disclose all the limitations of independent claim 1, this reference cannot anticipate claim 1 or any claims that depend from and include all the limitations of claim 1. Therefore, Chan *et al.* does not anticipate claims 2, 3, 11, and 13. Applicants respectfully

request withdrawal of the rejection of claims 1-3, 11, and 13 under 35 U.S.C. § 102(b).

Claim 17 is included in the rejection as allegedly anticipated by Chan *et al.* Claim 17 depends from claim 14, which is directed to "a substrate coated with a compound comprising an epoxy group as an active group one which a protein that interacts with a sugar chain has been immobilized, and in which one or more reaction vessels have been formed by affixing a rubber having one or more holes onto a glass." Chan *et al.* does not disclose a substrate in which one or more reaction vessels have been formed. Therefore, for at least this reason, Chan *et al.* does not anticipate claim 17 and Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 102(b).

Claim Rejections – 35 U.S.C. § 103

Claim 12 is rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Chan *et al.* in view of Mir (US 2004/0248144). Applicants traverse to the extent the rejection is maintained in view of the amendments herein.

As discussed above, Chan *et al.* does not describe "contacting a *fluorescently labeled subject sugar chain or subject glycoconjugate* with a substrate onto which a protein that interacts with a sugar chain has been immobilized…" Nor does Chan *et al.* describe "digitizing the fluorescence intensity and quantifying the fluorescence intensity." Mir does not remedy this deficiency. Mir describes a method of single molecule counting that identifies the presence or absence of a signal at a particular location (see, *e.g.,* Mir, paragraphs [0245]-[0251]). This does not include "quantifying the fluorescence intensity" as in Applicants' amended claim 1. Furthermore, Mir merely describes use of evanescent waves as excitation light as one of a number of methods of detecting a fluorescent signal (*e.g.,* Mir, paragraph [0225]). Mir does not disclose that evanescent wave excitation can be used without washing of the substrate, as in Applicants' claims. This provides a significant advantage, particularly in detecting and quantifying lectin-sugar chain interactions, due to the weak nature of those interactions (*e.g.,* specification, paragraphs [0008] and [0020]-[0021]).

Based on the foregoing, it is clear that the combination of Chan *et al.* and Mir *et al.* do not teach all the limitations of claim 12. Furthermore, one of skill in the art would not be motivated to combine the teachings of Chan *et al.* and Mir *et al.* with common general knowledge to arrive at Applicants' claimed method. Therefore, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

Claims 14 and 15 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Chan in view of Brennan (US 2003/0232382). Applicants traverse and request reconsideration.

The Office asserts that Brennan *et al.* teach that it is well known in the art to use materials such as rubber to separate reactants of one reaction area from those of another area (Office action, page 4, second paragraph). However, Brennan *et al.* do not describe utilizing rubber to separate reaction areas. Brennan *et al.* describe microfabricating wells on solid support (paragraph [0134]). Microfabricating wells on a solid support involves etching the surface to form the well. Brennan *et al.* also describe using a liquid to separate reactants or methods of chemically or photolytically treating a support surface to separate reactants (paragraph [0134]). None of these methods involve utilizing rubber (particularly rubber having one or more holes) affixed to a substrate to form one or more wells, as in Applicants' claims. Finally, Brennan *et al.* describe utilizing a liquid polymer "as a seal between two arrays or between individual reactions *to prevent excess solvent evaporation*" (paragraph [0134], emphasis added). Furthermore, Applicants' claimed substrate including affixing a rubber having one or more holes on the substrate provides adaptability of the array in that the reaction wells need not be pre-determined during the fabrication of an array. This allows production of differing number and formation of wells for different desired experiments utilizing the same underlying format of immobilized proteins that interact with a sugar chain. Brennan *et al.* do not teach using rubber to separate reaction areas and do not suggest the advantages of Applicants' claimed substrate "in which one or more reaction vessels have been formed by affixing a rubber having one or more holes onto a glass." Therefore, claims 14 and 15 are not unpatentable over Chan *et al.* in view of Brennan *et al.* and Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 103(a).

Conclusion

Applicants respectfully submit that the claims are now in condition for allowance. If any issues remain, the Examiner is requested to contact the undersigned to arrange a telephonic interview prior to the preparation of any further written action.

Respectfully submitted,

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